

Notice

Our file number: 12-110850-902

Re: Guidance Document: Preparation of Drug Regulatory Activities in the Common Technical Document (CTD) Format

Health Canada is pleased to announce the finalisation of the *Guidance Document: Preparation of Drug Regulatory Activities in the Common Technical Document (CTD) Format*.

This guidance document will assist sponsors in the preparation of drug regulatory activities in the Common Technical Document (CTD) format developed by the International Conference on Harmonisation (ICH). It defines the regional requirements of regulatory activities in CTD format, found in Modules 1 and 3.

The revised guidance document reflects comments received from stakeholders, including industry representatives. Those comments are collected in an issues analysis document, which includes changes made to the document in response to the comments.

Health Canada welcomes regulatory activities using the new Module 1 in CTD format at this time; however, the new Module 1 will not be accepted in electronic Common Technical Document (eCTD) format until the fall of 2012. Once a product has been moved to the new Module 1 format, it may not be reverted to the old Module 1. As of January 2013, Health Canada will no longer be accepting regulatory activities using the old Module 1.

In conjunction with this initiative, it should be noted that the draft *Guidance for Industry: Creation of the Canadian Module 1 eCTD Backbone File and the Document Type Definition (DTD) for the Canadian Module 1* have been updated and posted on the Health Canada website. The Clinical Trial Applications (CTA) guidance document is also being updated.

These guidance documents are meant to be read in conjunction with the most recent version of the CTD guidance documents and the corresponding *Questions and Answers* documents on the ICH website. It is also necessary for sponsors to consult relevant Health Canada and ICH-adopted guidance documents regarding content (data) requirements.

Any updates to CTD-related filing requirements will only be introduced following advance notice and will not be applied retroactively to regulatory activities pending review. Furthermore, for regulatory activities currently in preparation applicants may continue to follow the Health Canada guidelines/templates in effect prior to the date of release of this guidance document. Subsequent regulatory activity, however, should be compiled using the most recent guidelines.

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Questions concerning general filing requirements for CTD formatted submissions and the possible need for a pre-submission meeting should be directed to:

For Biologics and Genetic Therapies Directorate (BGTD) submissions:

Office of Regulatory Affairs
Biologics and Genetic Therapies Directorate
Fax: (613) 946-9520
BGTD_ORA @hc-sc.gc.ca

For Therapeutic Products Directorate (TPD) Submissions:

Regulatory Project Management Division
Office of Business Transformation
Therapeutic Products Directorate
Fax: (613) 957-1483
RPM_Division-GPR_Division@hc-sc.gc.ca



Health Canada Santé Canada

GUIDANCE DOCUMENT

Preparation of Drug Regulatory Activities in the Common
Technical Document (CTD) Format

Published by authority of the
Minister of Health

Date Adopted	2012/05/25
Effective Date	2012/06/22

Health Products and Food Branch

Canada

<p>Our mission is to help the people of Canada maintain and improve their health.</p> <p style="text-align: right;"><i>Health Canada</i></p>	<p>The Health Products and Food Branch's mandate is to take an integrated approach to the management of the risks and benefits to health related products and food by:</p> <ul style="list-style-type: none"> • minimizing health risk factors to Canadians while maximizing the safety provided by the regulatory system for products and food; and • promoting conditions that enable Canadians to make healthy choices and providing information so that they can make informed decisions about their health. <p style="text-align: right;"><i>Products and Food Branch</i></p>
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Également disponible en français sous le titre : Ligne directrice : Préparation de activités réglementaires de drogues en format Common Technical Document (CTD)

FOREWORD

Guidance documents are meant to provide assistance to industry and health care professionals on **how** to comply with governing statutes and regulations. Guidance documents also provide assistance to staff on how Health Canada mandates and objectives should be implemented in a manner that is fair, consistent and effective.

Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches to the principles and practices described in this document **may be** acceptable provided they are supported by adequate justification. Alternate approaches should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

As a corollary to the above, it is equally important to note that Health Canada reserves the right to request information or material, or define conditions not specifically described in this document, in order to allow the Department to adequately assess the safety, efficacy or quality of a product. Health Canada is committed to ensuring that such requests are justifiable and that decisions are clearly documented.

This document should be read in conjunction with the accompanying notice and the relevant sections of other applicable guidance documents.

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1 INTRODUCTION

The *Common Technical Document for Registration of Pharmaceuticals for Human Use* (International Conference on Harmonisation [ICH] Topic M4) was adopted by Health Canada, in 2003, for use in the preparation of drug regulatory activities (submissions and applications).

The Common Technical Document (CTD) provides a globally harmonised format that is accepted in many regions, avoiding the need to compile different registration dossiers for different regulatory authorities. It is organized into five modules. Module 1 is region specific, while Modules 2, 3, 4, and 5 are intended to be common for all regions. A regional component is included in Module 3. The review of information provided in a well structured regulatory activity will improve the efficiency of the screening and review of that regulatory activity.

This guidance document has been updated to facilitate the use of a common format for the filing of regulatory activities and the management of information over the lifecycle of a product. Once finalized, this guidance document will supersede the 2003 *Draft Guidance for Industry: Preparation of New Drug Submissions in the CTD Format* and all other references to the layout of Modules 1 and/or 3.2.R, where extensive changes have been made to provide placeholders for regional documents throughout the lifecycle of the product.

It is important to note that the implementation and use of the CTD represents a work in progress, and it is expected that future refinements of this guidance will continue to be necessary as a result of experience gained. Amendments will also be undertaken as a result of the migration to and implementation of the eCTD.

1.1 Policy Objective

To facilitate the preparation of a drug regulatory activity, pursuant to Part C of the *Food and Drug Regulations*, in the CTD format.

1.2 Policy Statement

The *Food and Drug Regulations* provides regulatory requirements for the approval and sale of drugs in Canada and prohibits the sale of drugs unless the manufacturer has filed a regulatory activity that is satisfactory to the Minister. Although the regulations do not define format requirements, Health Canada has adopted the CTD format within the Canadian registration framework. This guidance document, once finalised, is to be used in the preparation of drug regulatory activities for human use filed to Health Canada.

1.3 Scope and Application

This guidance document applies to the preparation of all drug regulatory activities for human use, filed pursuant to the *Food and Drug Regulations*, including Clinical Trial Applications (CTA), their amendments (CTA-A) and Drug Master Files (DMF).

The CTD format is the expected format for all drug regulatory activities including drug/device combinations where the primary mechanism of action is drug-related. For cases where the combination product is classified as a device, the use of the CTD format for the drug component is encouraged. For medical devices, please see *Summary Technical Document for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices* (STED), developed by the Global Harmonization Task Force (GHTF).

2 GUIDANCE FOR IMPLEMENTATION

This document outlines the CTD format for the submission of information in relation to drugs for human use, which is filed over the lifecycle of that product in Canada. **Table 1** provides an overview of the presentation of the drug regulatory activity, outlining the modular structure and main headings, which should be used.

The CTD format also provides the structure for the eCTD format; therefore some documents are specific to the format in which a regulatory activity is submitted. For example, the Table of Contents is only required in the CTD format, where the Life Cycle Management Table is only required in the eCTD format.

The first draft of the CTD Guidance (2003) was for the use of the CTD format with New Drugs Submission (NDS) regulatory activities only. With this guidance, Health Canada has moved to a more inclusive approach for the CTD format, with the inclusion of documents that may only be submitted for specific regulatory activity types or upon request; therefore many sections and subsections may not be applicable for a given regulatory activity. When no information is required in a specific section or subsection, that section or subsection should be omitted. A rationale for the absence of information may be required and should be provided as a note to reviewer. The numbering of an omitted section should not be reused for another section.

The CTD Guidance indicates *where and how* available information is to be presented; however, it is not intended to indicate *what* is actually required. Therefore, when preparing a regulatory activity, it is necessary to consult relevant Health Canada guidance documents (including the adopted ICH guidelines) on technical (data) requirements. Applicants are advised to consult the Health Canada website for the latest updates on guidance documents.

This guidance is intended to be used in conjunction with the most recent version of the following documents:

- ICH CTD guidelines and the corresponding *Questions and Answers* documents on the ICH website;
- The accompanying Health Canada *Notice* for supplementary and/or interim guidance; and
- Related Health Canada guidance documents and notices on Quality and comparative bioavailability information.

For additional guidance, the applicant should consult the appropriate review Bureau in the Therapeutic Products Directorate (TPD) or the Office of Regulatory Affairs in the Biologics and Genetic Therapies Directorate (BGTD).

Table 1: Presentation of Information in the Common Technical Document (CTD) Format

Module Number	Title and Main Section Headings	Cross-Reference to Modules	Binder/Label colour	Number of Paper Copies
1 1.0 1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.A	Administrative and Product Information Correspondence Table of Contents (Modules 1 to 5) Administrative Information Product Information Health Canada Summaries Environmental Assessment Statement Regional Clinical Information Clinical Trial Application and Clinical Trial Application- Amendment Specific Requirements Appendix	2, 3, 4 and 5	Red	1*
2 2.1 2.2 2.3 2.4 2.5 2.6 2.7	Common Technical Document (CTD) Summaries CTD Table of Contents (Modules 2 to 5) CTD Introduction Quality Overall Summary Nonclinical Overview Clinical Overview Nonclinical Written and Tabulated Summaries Clinical Summary	2 to 5 2 to 5 3 2 and 4 2 and 5 2 and 4 5	Yellow	1*
3 3.1 3.2 3.3	Quality Table of Contents of Module 3 Body of Data Literature References		Blue	1*
4 4.1 4.2 4.3	Nonclinical Study Reports Table of Contents of Module 4 Study Reports Literature References		Green	1

5	Clinical Study Reports		Black	1
5.1	Table of Contents of Module 5			
5.2	Tabular Listing of All Clinical Studies			
5.3	Clinical Study Reports			
5.4	Literature References			

* For combination products that require a joint review an additional copy of Modules 1, 2, and 3 is required.

3 STRUCTURE OF DRUG REGULATORY ACTIVITIES IN THE COMMON TECHNICAL DOCUMENT (CTD) FORMAT

3.1 Module 1: Administrative and Product Information

Module 1 identifies placeholders, defined by the numerical items listed in the Module 1 Table of Contents (ToC), for all administrative and product information documentation. Sponsors should use their own discretion based on the number of documents being provided in a given folder in order to decide if those documents should be organized using subfolders.

Module 1.0 Correspondence

All correspondence-related documents submitted to Health Canada are to be placed in Module 1.0 unless otherwise indicated. Scientific information is not to be included in this Module.

Module 1.0.1 Cover Letter

Any data being submitted to Health Canada should be accompanied by a cover letter. The cover letter should clearly state what is being submitted, including reference to the request letter (if applicable) and a brief description of the package. For example, if a Periodic Safety Update Report (PSUR) is being submitted, one of the following types should be indicated in the cover letter:

- Requested AD HOC PSUR - submitted as a one-time request (the requestor should be specified in the cover letter);
- Voluntary PSUR - unsolicited information
- Requested Periodic PSUR - requested by Health Canada, for example (e.g.) follow-up to a Risk Management Plan (RMP) or post-authorization commitment;
- PSUR-C (confirmatory) - submitted to support the fulfilment of a Notice of Compliance with Conditions (NOC/c).

The cover letter should not contain any scientific information. The Question and Answer (Q and A) responses from Health Canada issued correspondence and the Note to Reviewer are assigned a specific location (1.0.4 and 1.0.7) and should not be included in the cover letter.

Any cross-referenced regulatory activity should be clearly stated in the cover letter, and the following information should be included:

- regulatory activity type;
- control number;
- brand name;
- manufacturer / applicant's name;
- Central Registry (CR) file number;
- Date the regulatory activity was approved.

Module 1.0.2 Life Cycle Management (LCM) Table

The Life Cycle Management (LCM) Table is a specific requirement for filing a regulatory activity in eCTD format, and should be placed in this section.

Module 1.0.3 Copy of Health Canada Issued Correspondence

A Copy of the Health Canada issued correspondence being responded to should be placed in this section. This includes (but is not limited to) the following:

- Clarifax (during screening or review);
- Notice of Deficiency (NOD);
- Notice of Non-Compliance (NON);
- Not Satisfactory Notice (NSN);
- Post-Notice of Compliance Letters (Post-NOC);
- No Objection Letter (NOL) comments;
- Screening Deficiency Notice (SDN).

Module 1.0.4 Health Canada Solicited Information

Solicited information is defined as information requested by Health Canada. Responses to these requests are to be provided in Question and Answer format, and placed in this section. The answers should summarize the response and cross-reference the supporting data that is to be placed in the appropriate Module of the regulatory activity. **No supporting data** is to be provided in this section.

Module 1.0.5 Meeting Information

Any meeting related information and documentation, with the exception of Pipeline and Reconsideration meetings, are to be placed in this section. This includes (but is not limited to) the following:

- meeting information package;
- proposed meeting agenda;
- presentation slides;
- meeting minutes.

Module 1.0.6 Request for Reconsideration Documentation

Any documentation required as part of the Request for Reconsideration process is to be placed in this section.

Module 1.0.7 General Note to Reviewer

The Note to Reviewer should be used to facilitate the review. These comments are **NOT** to be included in the cover letter.

Notes relating to the entire regulatory activity (e.g., advising that the product is referred to by a foreign trade name throughout the regulatory activity) should be placed in this section.

Notes relating to a specific section of the regulatory activity should be placed at the beginning of each pertinent section. For example, this note can be used to identify changes in a section and/or document.

Module 1.1 Table of Contents (ToC)

The Table of Contents (ToC) for the entire regulatory activity should be placed in this section. It should list all documents included in Modules 1-5.

Module 1.2 Administrative Information

Module 1.2.1 Application Forms

Completed and signed application forms should be placed in this section.

Module 1.2.2 Fee Forms

Completed fee forms should be placed in this section.

Module 1.2.3 Certification and Attestation Forms

Completed and signed forms are to be placed in this section. These include, but are not limited to, the following:

- Submission Certification Form
 - Required as per section C.08.005.1 of the *Food and Drug Regulations*. The use of company letterhead is preferred. Please see the Health Canada website for an example of appropriate wording.
 - To be signed and dated by the senior executive officer of the manufacturer in Canada and the medical or scientific director of the manufacturer. If the submission certification or any significant part of the certification was prepared by an agent authorized by the manufacturer, the submission certification must also be signed by that agent.
 - Responses to Screening Deficiency Notices, Notices of Noncompliance and Notices of Deficiency should include a revised submission certificate signed and dated as described above.
- Letter of Attestation
 - To be included for any regulatory activity that includes both paper and electronic versions of information, confirming that the content contained in the electronic regulatory activity is identical to the paper-based regulatory activity.
- Submission Disclosure Form (BGTD only)
- Certification of Electronic Signature (placeholder)
- Changes in Manufacturer's Name and/or Product Name Administrative Changes - Certification Form
- Attestation of Pristine Product Monograph
- Product Monograph Translation Certification Form
- Bovine Spongiform Encephalopathy (BSE)/Transmissible Spongiform Encephalopathy (TSE) Attestation Form
- Certification of Suitability to the Monographs of the European Pharmacopoeia (CEP) issued by the European Directorate for the Quality of Medicines and Healthcare (EDQM)
- Application Certification Form
- Statement of Commitment for Drug Master Files (DMF)

Module 1.2.4 Intellectual Property Information

Module 1.2.4.1 Patent Information

As per the *Patented Medicines (Notice of Compliance) Regulations (PM (NOC) Regulations)*, an applicant (that is [i.e.] first person) who files or who has filed a new drug submission or a supplement to a new drug submission may submit a patent list in relation to the submission or supplement for addition to the Patent Register by

filing a Form IV: Patent List within the time limits and according to the conditions set out in section 4 of the *PM (NOC) Regulations*.

A second person (i.e. subsequent entrant) must address all patents listed on the Patent Register for the Canadian reference product used to establish bioequivalence for the second person's submission by filing a Form V: Declaration Re: Patent List as per section 5 of the *PM (NOC) Regulations*. Documents relating to the Notice of Allegation, including proof of service and the Acknowledgement and Certification of Receipt of Information and Material form, are also to be placed in this section.

Module 1.2.4.2 Data Protection Information

C.08.004.1 of the *Food and Drug Regulations* provides a term of data protection to manufacturers of innovative drugs during which the Minister shall not approve a subsequent entry submission submitted for a new drug on the basis of a comparison between the new drug and the innovative drug. The term of data protection is effective from the date of the issuance of the Notice of Compliance (NOC) and extends to eight years (eight and one-half years if relevant paediatric clinical trial data is submitted). Innovative manufacturers may place information that supports the eligibility of their innovative drug for data protection in this section.

Module 1.2.5 Compliance and Site Information

Module 1.2.5.1 Clinical Trial Site Information Forms

Completed Clinical Trial Site Information Forms (CTSI) must be provided in this section for each proposed clinical trial site.

Module 1.2.5.2 Establishment Licensing

Establishment Licensing (EL) information should be placed in this section.

Module 1.2.5.3 Good Clinical Practices

Good Clinical Practices (GCP) related documentation should be placed in this section.

Module 1.2.5.4 Good Laboratory Practices

A statement of GLP compliance consistent with the Organisation for Economic Co-operation and Development's (OECD) *Principles of Good Laboratory Practice (GLP)* should be placed in this section.

Module 1.2.5.5 Good Manufacturing Practices

Good Manufacturing Practices (GMP) compliance information should be placed in this section. This may include the Certificate of Compliance (COC) issued by the Health Products and Food Branch Inspectorate (HPFBI) when the foreign GMP rating is accepted for a foreign site under a Mutual Recognition Agreement (MRA).

Regulatory GMP compliance and EL status issued by other jurisdictions, including Date of last GMP and/or pre-approval inspection, and any observation-related information should also be placed in this section.

Module 1.2.5.6 Good Pharmacovigilance Practices

Good Pharmacovigilance Practices (GPP) related documentation should be placed in this section.

Module 1.2.5.7 Other Compliance and Site Information Documents

Any other regulatory compliance and site-related information which is not currently covered under Module 1.2.5.1-1.2.5.6 should be placed in this section.

Module 1.2.6 Authorization for Sharing Information

Letters authorizing Health Canada to share information regarding the regulatory activity with other regulatory authorities (or vice versa), and/or to access other (third party) drug regulatory activities, DMF and Site Reference Files (SRF) should be provided in this section.

Module 1.2.7 International Information

Information on the product application, approved indications and marketing status in other countries/regions provide useful contextual information should be provided in this section when requested. Depending upon the status this may include, but not be limited to, the following:

- International registration, review and/or marketing status, including date of filing, approval of product or supplemental changes in other jurisdictions, information regarding the withdrawal, stop of sale and/or market recall;
- Foreign refusals;
- Foreign clinical trial status;
- International Birth Date of the product and for all approved indications;

- Confirmation of filing or the date(s) of approval or withdrawal;
- Foreign review reports, including Question and Answer (Q and A) documents (**upon request only**);
- Meeting minutes from other jurisdictions (**upon request only**).

Module 1.2.8 Post-Authorization Information

The following information should be included in this section:

- Market Notification Forms
 - As per part C.01.014.3 of the *Food and Drugs Regulations*, companies are required to notify Health Canada of a drug being sold.
 - For labels see section 1.3.2
- Post-Authorization Commitments
 - The commitment tracking table, as detailed in Appendix C should be provided here.
 - These commitments are intended for those outside of the NOC/c scope. For NOC/c related documents, see Module 1.6.4.
- Notices of Change (Level III) forms
 - *Post-Notice of Compliance (NOC) Changes: Notices of Change (Level III) Forms* are to be placed in this section. These forms should not be confused with the Annual Notification, which is not included in the scope of this document.
- Notice of Decision and Summary Basis of Decision
 - All versions of the Notice of Decision and Summary Basis of Decision documents are to be placed in this section.

Module 1.2.9 Other Administrative Information

This section is for any administrative information that does not have a designated location in the CTD format. This section should **NOT** contain any scientific information.

Module 1.3 Product Information

Module 1.3.1 Product Monograph

A copy of the non-annotated (clean) and annotated Product Monograph are to be placed in this section. This includes both the pristine and second language PMs.

The text of the annotated copy at the time of filing should be cross-referenced to supporting information and study findings reported in Module 2 documents and, when submitted, the Bioequivalence Summary (Module 1.4.2). Applicants may also choose to include references to related information in Modules 3 to 5, as appropriate.

Within the sections of the annotated Product Monograph, the text should also be cross-referenced by number to the *References or Selected Bibliography* section at the end of the Product Monograph.

Articles from publications listed in the References section should be cited in accordance with the current edition of the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals*, International Committee of Medical Journals Editors (ICMJE). When reference is made to a publication not provided in Modules 2 - 5, copies of the reference material should be provided in this section.

When revisions are requested during the course of the review, an annotated version of the revised Product Monograph is required. The annotations should reflect all changes made, either in relation to the last approved PM or in response to a request made from Health Canada.

Module 1.3.2 Inner and Outer Labels

All inner and outer labels should be provided in this section, including those submitted with the Market Notification.

This should include the labels for all strengths, dosage forms and reconstitution diluents. Typewritten or other draft label copy is acceptable for review purposes.

When additional revisions are requested during the course of the review, an annotated version of the revised label maybe requested, and should be placed in this section.

Module 1.3.3 Non-Canadian Labelling

If the drug product has been marketed outside Canada, the applicant is encouraged to supply the monograph or package inserts approved in other jurisdictions, clearly identifying them by country or region.

Module 1.3.4 Investigator's Brochure

Investigator's Brochure for CTA and CTA-As should be placed in this section.

Module 1.3.5 Reference Product Labelling

The Product Monograph for Canadian Reference Products is to be placed in this section.

Module 1.3.6 Certified Product Information Document

A copy of the non-annotated (clean) and annotated CPID are to be placed in this section. The text of the annotated copy at the time of filing should be cross-referenced to the corresponding sections of Module 3, while any further revisions should reflect all changes that have been made, including Level III changes. The clean version should not contain any cross-referencing.

Module 1.3.7 Look alike/Sound alike Assessments

The assessments are to be placed in this section.

Module 1.3.8 Pharmacovigilance Information

Module 1.3.8.1 Pharmacovigilance Plan

Pharmacovigilance plans or their equivalent are to be placed in this section.

Module 1.3.8.2 Risk Management Plan

Risk management plans or their equivalent are to be placed in this section.

Module 1.3.8.3 Risk Communications

Risk Communications are to be placed in this section.

Module 1.3.8.4 Other Pharmacovigilance Information

Any other pharmacovigilance information should be placed in this section.

Module 1.4 Health Canada Summaries

Module 1.4.1 PSEAT-CTA

The completed Protocol Safety and Efficacy Assessment Template - Clinical Trial Application should be placed in this section.

Module 1.4.2 Comprehensive Summary: Bioequivalence

The completed Comprehensive Summary: Bioequivalence (CS-BE) for all *pivotal* comparative bioavailability (bioequivalence) studies should be placed in this section.

Module 1.4.3 Multidisciplinary Tabular Summaries

This section is a placeholder for tables that contain information that is applicable to more than one discipline.

Module 1.5 Environmental Assessment Statement

An Environmental Assessment Statement is required for new substances in products regulated under the *Food and Drug Act* as per the New Substances Notification Regulations (NSN) of the *Canadian Environmental Protection Act* (CEPA). As per the New Substances Program Advisory Note 2006-04, New Substance Notification (NSN) packages for substances used in product regulated by the Food and Drugs Act must be submitted to the New Substances Division at Environment Canada.

Module 1.6 Regional Clinical Information

Module 1.6.1 Comparative Bioavailability Information

Specific requirements for *pivotal* comparative bioavailability (bioequivalence) studies should be placed in this section. These specific requirements include, but are not limited to:

- Canadian Reference Product (CRP) Confirmation;
- Requests for waivers and justification statements;
- Verification of potency of the Test and Reference products (Certificates of Analysis);
- Bioavailability/Bioequivalence (BA/BE) data sets (required for all types of *pivotal* comparative bioavailability (bioequivalence) studies).

Module 1.6.2 Company Core Data Sheets

Company Core Data Sheets should be placed in this section.

Module 1.6.3 Priority Review Requests

All documents related to a Priority Review Request should be placed in this section only.

Module 1.6.4 Notice of Compliance with Conditions

All documentation relating to an NOC/c is to be placed in this section only. These documents include, but are not limited to, the following:

- Letter of undertaking;
- Qualifying Notice;
- Dear Health Care Professional Letters (DHCPL);
- Product Specific Fact Sheets.

Module 1.7 Clinical Trial Information

Module 1.7.1 Study Protocol

All required copies of the Study Protocol are to be placed in this section.

Module 1.7.2 Informed Consent Forms

The Informed Consent Forms are to be placed in this section.

Module 1.7.3 Canadian Research Ethics Board (REB) Refusals

Canadian Research Ethics Board (REB) refusals are to be placed in this section.

Module 1.7.4 Information on Prior-related Applications

Information on prior-related applications is to be placed in this section.

Module 1.A Appendix

Module 1.A.1 Electronic Review Documents

All electronic media submitted to support the drug regulatory activity should be placed in this section.

3.2 Module 2: Common Technical Document (CTD) Summaries

Please consult the ICH M4 Guidelines.

3.3 Module 3: Quality

Please consult the ICH M4Q Guidelines.

Module 3.2.R Regional Information

To complete the regional section of Module 3 the applicant should refer to the appropriate Health Canada CTD Quality guidance documents.

Module 3.2.R.1 Production Documentation

Module 3.2.R.2 Medical Devices

Module 3.2.R.3 Lot Release Documentation - BGTD

Module 3.2.R.4 Yearly Biologic Product Report (YBPR)-BGTD Only

The Yearly Biologic Product Report (YBPR), provided for BGTD only, is to be placed in this section.

3.4 Module 4: Nonclinical Study Reports

The applicant should refer to the ICH M4S guidelines, as well as the appropriate Health Canada guidance documents to complete this module.

3.5 Module 5: Clinical Study Reports

The applicant should refer to the ICH M4E guideline under *Module 5: Clinical Study Reports*, and the ICH E3 guideline, *Structure and Content of Clinical Study Reports*.

In addition, the applicant should note the following in relation to cited modules of the CTD:

Module 5.3.1.2 Comparative Bioavailability (BA) / Bioequivalence (BE) Study Reports

The technical requirements for *pivotal* comparative bioavailability (bioequivalence) studies are provided in the Health Canada *Guidance for Industry: Preparation of Comparative Bioavailability Information for Drug Submissions in the CTD Format*.

Module 5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies

The technical requirements for *pivotal* comparative bioavailability (bioequivalence) studies are provided in the Health Canada *Guidance for Industry: Preparation of Comparative Bioavailability Information for Drug Submissions in the CTD Format*.

Module 5.3.6 Post Marketing Experience

Periodic Safety Update Reports (PSUR) should be placed in this section.

Module 5.3.7 Case Report Forms and Individual Patient Listings

Case report forms that are described as appendix 13.3.1 in the ICH clinical study report guideline (E3) should be placed in this section at the time of filing.

Appendices 16.3.2 (Other Case Report Forms (CRFs)) and 16.4 (Individual patient Data Listings) are to be sent promptly (within 2 business days) when requested.

All CRFs provided should be placed in this section, in the same order as the clinical study reports, and indexed by study. All CRFs are to be provided in electronic format only.

4 PRESENTATION OF REGULATORY ACTIVITIES

This section describes the physical specifications for submitting paper regulatory activity in CTD format. The paper format is to serve as the official Central Registry (legal) copy for paper-based regulatory activity.

4.1 Organization and Identification of Regulatory Activity Volumes

- The regulatory activity should be bound in three-ring binders.
- Binders should be colour-coded as specified in **Table 1**. Alternatively, labels on the spines as well as on the cover are to be colour-coded as indicated.
- The binder labels on the spine and the front cover should include the following information:
 - trade (brand) name of the drug product;
 - name of the manufacturer;
 - proper or common and code names;
 - sequential number, starting at Volume 1 for each module;
 - The volume number for that binder, out of the total number of volumes for that module, the section(s) contained within each volume, and the date of regulatory activity (month and year), should also be specified on the label.

For example, the label on a blue-coloured binder (Volume 1 of Module 3: Quality), would read as follows:

Drug Product “ABC”
Applicant/Manufacturer “XYZ”
Volume 1 of 63
3.1-3.2.S.2.3
Month/year

Note: In the case of Notifiable Changes (NCs) containing small amounts of information it is recommended, where possible, that all modules of the regulatory activity be provided in one (black) binder.

4.2 Organization, Presentation and Identification of Information within Regulatory Activities

Information within the CTD is organized into a series of structured documents which are in turn organized into modules. The M4 guidance *Organisation of the Common Technical Document* and ICH General *Questions and Answers* provides the definition of a document and guidance on

ToC formatting, cross-referencing within the CTD and for document pagination, segregation and section numbering.

Literature references should be cited in accordance with the current edition of the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals*, International Committee of Medical Journals Editors (ICMJE).

Acronyms and abbreviations should be defined the first time they are used in each module.

Module 1 does not need to be paginated in full, but pagination within documents is useful. It is not necessary to include a header or footer on Module 1 documents, except where already an integral part of the document, (e.g. the Certified Product Information Document (CPID) template), or to paginate Module 1 forms or labels.

4.3 Language

Information in the regulatory activity should be recorded in either English or French. Material in a different language should be accompanied by an English or French translation with the possible exception of Case Report Forms (consult the appropriate Bureau (TPD) or the Office of Regulatory Affairs (BGTD) first).

4.4 Legibility and Font Size

Text and tables should be prepared using margins that allow the document to be printed on 8.5 x 11 inch paper. The left-hand margin should be sufficiently large that information is not obscured by the method of binding. Font sizes for text, tables, flow diagrams and floor maps should be of a style and size that are large enough to be easily legible, even after photocopying. Times New Roman, 12-point font is recommended for narrative text.

5 APPENDICES

APPENDIX A: CANADIAN MODULE 1

Module #	Module Title
1	Administrative and Product Information
1.0	Correspondence
1.0.1	Cover letter
1.0.2	Life Cycle Management Table
1.0.3	Copy of Health Canada issued correspondence
1.0.4	Health Canada Solicited Information
1.0.5	Meeting Information

1.0.6	Request for Reconsideration Documentation
1.0.7	General Note to Reviewer
1.1	Table of Contents
1.2	Administrative Information
1.2.1	Application Forms
1.2.2	Fee Forms
1.2.3	Certification and Attestation Forms
1.2.4	Intellectual Property Information
1.2.4.1	Patent Information
1.2.4.2	Data Protection Information
1.2.5	Compliance and Site Information
1.2.5.1	Clinical Trial Site Information Form
1.2.5.2	Establishment Licensing
1.2.5.3	Good Clinical Practices
1.2.5.4	Good Laboratory Practices
1.2.5.5	Good Manufacturing Practices
1.2.5.6	Good Pharmacovigilance Practices
1.2.5.7	Other Compliance and Site Information Documents
1.2.6	Authorization for Sharing Information
1.2.7	International Information
1.2.8	Post- Authorization Information
1.2.9	Other Administrative Information
1.3	Product Information
1.3.1	Product Monograph
1.3.2	Inner and Outer Labels
1.3.3	Non-Canadian Labelling
1.3.4	Investigator's Brochure
1.3.5	Reference Product Labelling
1.3.6	Certified Product Information Document
1.3.7	Look-alike/Sound-alike Assessment
1.3.8	Pharmacovigilance Information
1.3.8.1	Pharmacovigilance Plan
1.3.8.2	Risk Management Plan
1.3.8.3	Risk Communications
1.3.8.4	Other Pharmacovigilance Information
1.4	Health Canada Summaries
1.4.1	PSEAT-CTA
1.4.2	Comprehensive Summary : Bioequivalence
1.4.3	Multidisciplinary Tabular Summaries
1.5	Environmental Assessment Statement

1.6	Regional Clinical Information
1.6.1	Comparative Bioavailability Information
1.6.2	Company Core Data Sheets
1.6.3	Priority Review Requests
1.6.4	Notice of Compliance with Conditions
1.7	Clinical Trial Information
1.7.1	Study Protocol
1.7.2	Informed Consent Forms
1.7.3	Canadian Research Ethics Board (REB) Refusals
1.7.4	Information on Prior-related Applications
1.A	Appendix
1.A.1	Electronic Review Package

APPENDIX B: CORRELATION OF ORIGINAL VERSUS PROPOSED MODULE 1

Original		Proposed	
Module #	Module Title	Module #	Module Title
1	Administrative Information and Prescribing Information	1	Administrative and Product Information
		1.0	Correspondence
		1.0.1	Cover letter
		1.0.2	Life Cycle Management Table
		1.0.3	Copy of Health Canada issued correspondence
		1.0.4	Health Canada Solicited Information
		1.0.5	Meeting Information
		1.0.6	Request for Reconsideration Documentation
		1.0.7	General Note to Reviewer
1.1	Table of Contents	1.1	Table of Contents
1.2	Application Information	1.2	Administrative Information
1.2.1	Drug Submission Application Form (HC-SC 3011)	1.2.1	Application Forms
1.2.2	Drug Submission Fee Application Form	1.2.2	Fee Forms
1.2.3	Submission Certification Form	1.2.3	Certification and Attestation Forms
1.2.4	Patent Information	1.2.4	Intellectual Property Information
		1.2.4.1	Patent Information
		1.2.4.2	Data Protection Information
1.2.5	Good Manufacturing Practices (GMP) and Establishment Licensing (EL) Information	1.2.5	Compliance and Site Information
		1.2.5.1	Clinical Trial Site Information Form
		1.2.5.2	Establishment Licensing
		1.2.5.3	Good Clinical Practices
		1.2.5.4	Good Laboratory Practices
		1.2.5.5	Good Manufacturing Practices
		1.2.5.6	Good Pharmacovigilance Practices
		1.2.5.7	Other Compliance and Site Information Documents
1.2.6	Letter of Access	1.2.6	Authorization for Sharing Information

Original		Proposed	
1.2.7	International Registration Status	1.2.7	International Information
1.2.8	Other Application Information	1.2.8	Post-Authorization Information
		1.2.9	Other Administrative Information
1.3	Product Labelling	1.3	Product Information
1.3.1	Product Monograph	1.3.1	Product Monograph
1.3.2	Inner and Outer Labels	1.3.2	Inner and Outer Labels
1.3.3	Non-Canadian Package Inserts	1.3.3	Non-Canadian Labelling
		1.3.4	Investigator's Brochure
		1.3.5	Reference Product Labelling
		1.3.6	Certified Product Information Document
		1.3.7	Look-alike/Sound-alike Assessment
		1.3.8	Pharmacovigilance Information
		1.3.8.1	Pharmacovigilance Plan
		1.3.8.2	Risk Management Plan
		1.3.8.3	Risk Communications
		1.3.8.4	Other Pharmacovigilance Information
1.4	Health Canada Summaries	1.4	Health Canada Summaries
1.4.1	Certified Product Information Document (CPID)	1.4.1	PSEAT-CTA
1.4.2	Comprehensive Summary: BioEquivalence	1.4.2	Comprehensive Summary : Bioequivalence
		1.4.3	Multidisciplinary Tabular Summaries
1.5	Environmental Assessment Statement	1.5	Environmental Assessment Statement
1.6	Electronic Review Documents	1.6	Regional Clinical Information
		1.6.1	Comparative Bioavailability Information
		1.6.2	Company Core Data Sheets
		1.6.3	Priority Review Requests
		1.6.4	Notice of Compliance with Conditions
		1.7	Clinical Trial Information
		1.7.1	Study Protocol
		1.7.2	Informed Consent Forms
		1.7.3	Canadian Research Ethics Board (REB) Refusals

Original		Proposed	
		1.7.4	Information on Prior-related Applications
		1.A	Appendices
		1.A.1	Electronic Review Package

APPENDIX C: POST-AUTHORIZATION COMMITMENTS

Commitments are periodically made by the sponsors to provide additional information to Health Canada in order to further support the approved regulatory activity.

Regulatory activities with Post-Authorization commitments should be tracked. These Post-Authorization commitments are not subject to the NOC/c policy, either because they do not meet the requirements or because they are Level II changes.

Some examples include (but are not limited to) the following:

- additional stability data;
- periodic updates of ongoing trials or surveillance programs;
- risk management studies (e.g. phase IV, pharmacoepidemiological, drug utilization studies).

To track the status of outstanding commitments over the Lifecycle of the product, the following table should be included in section 1.2.8 Post- Authorization Information.

Summary of Commitment	Date of No Objection Letter/ Notice of Compliance	Control #	Date Outstanding Information Provided	Date of commitment closure by Health Canada

Once the commitment has been closed off by Health Canada, it should remain in the table for at least one subsequent regulatory activity, after which it can be removed.

If there are no commitments open, and all previous commitments have met the conditions described above, a table does not need to be provided.

APPENDIX D: COMMON TECHNICAL DOCUMENT (CTD) FORMAT

Module Number and Section Heading

- 1 Administrative and Product Information**
- 1.0 Correspondence
- 1.0.1 Cover letter
- 1.0.2 Life Cycle Management Table
- 1.0.3 Copy of Health Canada issued correspondence
- 1.0.4 Health Canada Solicited Information
- 1.0.5 Meeting Information

- 1.0.6 Request for Reconsideration Documentation
- 1.0.7 General Note to Reviewer
- 1.1 Table of Contents
- 1.2 Administrative Information
 - 1.2.1 Application Forms
 - 1.2.2 Fee Forms
 - 1.2.3 Certification and Attestation Forms
 - 1.2.4 Intellectual Property Information
 - 1.2.4.1 Patent Information
 - 1.2.4.2 Data Protection Information
 - 1.2.5 Compliance and Site Information
 - 1.2.5.1 Clinical Trial Site Information Form
 - 1.2.5.2 Establishment Licensing
 - 1.2.5.3 Good Clinical Practices
 - 1.2.5.4 Good Laboratory Practices
 - 1.2.5.5 Good Manufacturing Practices
 - 1.2.5.6 Good Pharmacovigilance Practices
 - 1.2.5.7 Other Compliance and Site Information Documents
 - 1.2.6 Authorization for Sharing Information
 - 1.2.7 International Information
 - 1.2.8 Post- Authorization Information
 - 1.2.9 Other Administrative Information
- 1.3 Product Information
 - 1.3.1 Product Monograph
 - 1.3.2 Inner and Outer Labels
 - 1.3.3 Non-Canadian Labelling
 - 1.3.4 Investigator's Brochure
 - 1.3.5 Reference Product Labelling
 - 1.3.6 Certified Product Information Document
 - 1.3.7 Look-alike/Sound-alike Assessment
 - 1.3.8 Pharmacovigilance Information
 - 1.3.8.1 Pharmacovigilance Plan
 - 1.3.8.2 Risk Management Plan
 - 1.3.8.3 Risk Communications
 - 1.3.8.4 Other Pharmacovigilance Information
- 1.4 Health Canada Summaries
 - 1.4.1 PSEAT-CTA
 - 1.4.2 Comprehensive Summary: Bioequivalence
 - 1.4.3 Multidisciplinary Tabular Summaries
- 1.5 Environmental Assessment Statement
- 1.6 Regional Clinical Information
 - 1.6.1 Comparative Bioavailability Information

- 1.6.2 Company Core Data Sheets
- 1.6.3 Priority Review Requests
- 1.6.4 Notice of Compliance with Conditions
- 1.7 Clinical Trial Information
 - 1.7.1 Study Protocol
 - 1.7.2 Informed Consent Forms
 - 1.7.3 Canadian Research Ethics Board (REB) Refusals
 - 1.7.4 Information on Prior-related Applications
- 1.A Appendix
 - 1.A.1 Electronic Review Package

- 2 Common Technical Document Summaries**
 - 2.1 Common Technical Document Table of Contents (Modules 2-5)
 - 2.2 Introduction
 - 2.3 Quality Overall Summary
 - 2.4 Nonclinical Overview
 - 2.5 Clinical Overview
 - 2.6 Nonclinical Summary and Tabulated Summaries
 - 2.7 Clinical Summary

- 3 Quality**
 - 3.1 Table of Contents of Module 3
 - 3.2 Body of Data
 - 3.2.S Drug Substance
 - 3.2.S.1 General Information
 - 3.2.S.1.1 Nomenclature
 - 3.2.S.1.2 Structure
 - 3.2.S.1.3 General Properties
 - 3.2.S.2 Manufacture
 - 3.2.S.2.1 Manufacturer(s)
 - 3.2.S.2.2 Description of Manufacturing Process and Process Controls
 - 3.2.S.2.3 Control of Materials
 - 3.2.S.2.4 Controls of Critical Steps and Intermediates
 - 3.2.S.2.5 Process Validation and/or Evaluation
 - 3.2.S.2.6 Manufacturing Process Development
 - 3.2.S.3 Characterisation
 - 3.2.S.3.1 Elucidation of Structure and other Characteristics
 - 3.2.S.3.2 Impurities
 - 3.2.S.4 Control of Drug Substance
 - 3.2.S.4.1 Specification
 - 3.2.S.4.2 Analytical Procedures
 - 3.2.S.4.3 Validation of Analytical Procedures

- 3.2.S.4.4 Batch Analyses
- 3.2.S.4.5 Justification of Specification
- 3.2.S.5 Reference Standards or Materials
- 3.2.S.6 Container Closure System
- 3.2.S.7 Stability
 - 3.2.S.7.1 Stability Summary and Conclusions
 - 3.2.S.7.2 Post-approval Stability Protocol and Stability Commitment
 - 3.2.S.7.3 Stability Data
- 3.2.P Drug Product
 - 3.2.P.1 Description and Composition of the Drug Product
 - 3.2.P.2 Pharmaceutical Development
 - 3.2.P.3 Manufacture
 - 3.2.P.3.1 Manufacturer(s)
 - 3.2.P.3.2 Batch Formula
 - 3.2.P.3.3 Description of Manufacturing Process and Process Controls
 - 3.2.P.3.4 Controls of Critical Steps and Intermediates
 - 3.2.P.3.5 Process Validation and/or Evaluation
 - 3.2.P.4 Control of Excipients
 - 3.2.P.4.1 Specifications
 - 3.2.P.4.2 Analytical Procedures
 - 3.2.P.4.3 Validation of Analytical Procedures
 - 3.2.P.4.4 Justification of Specifications
 - 3.2.P.4.5 Excipients of Human or Animal Origin
 - 3.2.P.4.6 Novel Excipients
 - 3.2.P.5 Control of Drug Product
 - 3.2.P.5.1 Specification(s)
 - 3.2.P.5.2 Analytical Procedures
 - 3.2.P.5.3 Validation of Analytical Procedures
 - 3.2.P.5.4 Batch Analyses (For BGTD): Batch Analyses (For TPD):
 - 3.2.P.5.5 Characterisation of Impurities
 - 3.2.P.5.6 Justification of Specification(s)
 - 3.2.P.6 Reference Standards or Materials
 - 3.2.P.7 Container Closure System
 - 3.2.P.8 Stability
 - 3.2.P.8.1 Stability Summary and Conclusions
 - 3.2.P.8.2 Post-approval Stability Protocol and Stability Commitment
 - 3.2.P.8.3 Stability Data
- 3.2.A Appendices
 - 3.2.A.1 Facilities and Equipment
 - 3.2.A.2 Adventitious Agents Safety Evaluation
 - 3.2.A.3 Excipients
- 3.2.R Regional Information

- 3.2.R.1 Production Documentation
- 3.2.R.2 Medical Devices
- 3.2.R.3 Lot Release Documentation (for BGTD)
- 3.2.R.4 Yearly Biologic Product Reports (BGTD only)
- 3.3 Literature References

4 Nonclinical Study Reports

- 4.1 Table of Contents of Module 4
- 4.2 Study Reports
 - 4.2.1 Pharmacology
 - 4.2.1.1 Primary Pharmacodynamics
 - 4.2.1.2 Secondary Pharmacodynamics
 - 4.2.1.3 Safety Pharmacology
 - 4.2.1.4 Pharmacodynamic Drug Interactions
 - 4.2.2 Pharmacokinetics
 - 4.2.2.1 Analytical Methods and Validation Reports (if separate reports are available)
 - 4.2.2.2 Absorption
 - 4.2.2.3 Distribution
 - 4.2.2.4 Metabolism
 - 4.2.2.5 Excretion
 - 4.2.2.6 Pharmacokinetic Drug Interactions (nonclinical)
 - 4.2.2.7 Other Pharmacokinetic Studies
 - 4.2.3 Toxicology
 - 4.2.3.1 Single-Dose Toxicity (in order by species, by route)
 - 4.2.3.2 Repeat-Dose Toxicity
 - 4.2.3.3 Genotoxicity
 - 4.2.3.3.1 *In vitro*
 - 4.2.3.3.2 *In vivo* (supportive toxicokinetics evaluations)
 - 4.2.3.4 Carcinogenicity (including toxicokinetics)
 - 4.2.3.4.1 Long-term studies (not included in repeat-dose toxicity or pharmacokinetics)
 - 4.2.3.4.2 Short- or medium-term studies (not included under repeat-dose toxicity or pharmacokinetics)
 - 4.2.3.4.3 Other studies
 - 4.2.3.5 Reproductive and Developmental Toxicity
 - 4.2.3.5.1 Fertility and early embryonic development
 - 4.2.3.5.2 Embryo-fetal development
 - 4.2.3.5.3 Prenatal and postnatal development, including maternal function
 - 4.2.3.5.4 Studies in which the offspring (juvenile animals) are dosed and/or further evaluated
 - 4.2.3.6 Local Tolerance
 - 4.2.3.7 Other Toxicity Studies (if available)
 - 4.2.3.7.1 Antigenicity

- 4.2.3.7.2 Immunotoxicity
- 4.2.3.7.3 Mechanistic studies (if not included elsewhere)
- 4.2.3.7.4 Dependence
- 4.2.3.7.5 Metabolites
- 4.2.3.7.6 Impurities
- 4.2.3.7.7 Other
- 4.3 Literature References

- 5 Clinical Study Reports**
- 5.1 Table of Contents of Module 5
- 5.2 Tabular Listing of Clinical Studies
- 5.3 Clinical Study Reports
 - 5.3.1 Reports of Biopharmaceutical Studies
 - 5.3.1.1 Bioavailability Study Reports
 - 5.3.1.2 Comparative Bioavailability and Bioequivalence Study Reports
 - 5.3.1.3 *In vitro-In vivo* Correlation Study Reports
 - 5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies
 - 5.3.2 Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials
 - 5.3.2.1 Plasma Protein Binding Study Reports
 - 5.3.2.2 Reports of Hepatic Metabolism and Drug Interaction Studies
 - 5.3.2.3 Reports of Studies Using Other Human Biomaterials
 - 5.3.3 Reports of Human Pharmacokinetic Studies
 - 5.3.3.1 Healthy Subject PK and Initial Tolerability Study Reports
 - 5.3.3.2 Patient PK and Initial Tolerability Study Reports
 - 5.3.3.3 Intrinsic Factor PK Study Reports
 - 5.3.3.4 Extrinsic Factor PK Study Reports
 - 5.3.3.5 Population PK Study Reports
 - 5.3.4 Reports of Human Pharmacodynamic Studies
 - 5.3.4.1 Healthy Subject PD and PK/PD Study Reports
 - 5.3.4.2 Patient PD and PK/PD Study Reports
 - 5.3.5 Reports of Efficacy and Safety Studies
 - 5.3.5.1 Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication
 - 5.3.5.2 Study Reports of Uncontrolled Clinical Studies References
 - 5.3.5.3 Reports of Analyses of Data from more than one study, including any formal integrated analyses, meta-analyses, and bridging analyses
 - 5.3.5.4 Other Clinical Study Reports
 - 5.3.6 Reports of Postmarketing Experience
 - 5.3.7 Case Report Forms and Individual Patient Listings (when submitted)
- 5.4 Literature References

6 REFERENCES

6.1 Health Canada References

The latest versions of these and other Health Canada guidance documents, policies, templates and forms that should be consulted during the preparation of a drug regulatory activity can be obtained from Health Canada's TPD web page (<http://www.hc-sc.gc.ca/dhp-mps/prodpharma/index-eng.php>) and BGTD web page (<http://www.hc-sc.gc.ca/dhp-mps/brgtherap/index-eng.php>).

List of documents available on the Health Canada website:

- Guidance for Industry: Management of Drug Submissions;
- Guidance for Industry: Preparation of a Drug Submission in Electronic Common Technical Document (eCTD) Format;
- Guidance for Industry: Reconsideration of Final Decisions Issued for Human Drug Submissions;
- Guidance Document on Cost Recovery Submission Evaluation Fees;
- Draft Guidance Document: Drug Master Files (DMF);
- Drug Good Manufacturing Practices (GMP), and the Establishment Licensing Enforcement Directive (POL-0004);
- Good Manufacturing Practices (GMP) Guidelines;
- Notice: Submission Filing Requirements - Good Manufacturing Practices (GMP) / Establishment Licences (EL);
- Guidance document Non-Clinical Laboratory Study Data Supporting Drug Product Applications and Submissions: Adherence to Good Laboratory Practice;
- Guidance for Industry Product Monograph;
- Guidance for Industry: Drug Name Review: Look-alike Sound-alike (LA/SA) Health Product Names;
- Guidance for Industry: Priority Review of Drug Submissions;
- Guidance for Industry: Notice of Compliance with Conditions;
- Quality Guidance: New Drug Submissions (NDSs) and Abbreviated New Drug Submissions (ANDSs) for Chemical Entities (products containing drugs of synthetic or semi-synthetic origin, excluding Schedule C and D drugs);
- Notice: Revised Quality Guidances on the Implementation of the Common Technical Document for Biological Products;
- Preparation of the Quality Information for Drug Submissions in the CTD Format: Biotechnological/ Biological (Biotech) Products;
- Preparation of the Quality Information for Drug Submissions in the CTD Format: Blood Products;
- Preparation of the Quality Information for Drug Submissions in the CTD Format:

Conventional Biotherapeutic Products;

- Preparation of the Quality Information for Drug Submissions in the CTD Format: Vaccines;
- Guidance for Industry: Preparation of Comparative Bioavailability Information for Drug Submissions in the CTD Format;
- Notice Regarding Implementation of Risk Management Planning including the adoption of International Conference on Harmonisation (ICH) Guidance Pharmacovigilance Planning - ICH Topic E2E;
- Guidance for Clinical Trial Sponsors - Clinical Trial Applications;
- Post-Notice of Compliance (NOC) Changes Guidance Documents;
- Guidance for Sponsors: Lot Release Program for Schedule D (Biologic) Drugs;
- Guidance for Sponsors: Information and Submission Requirements for Subsequent Entry Biologics (SEBs);
- Notice: Common Technical Document - ICH Topic M4.

The ICH M4 guidelines adopted by Health Canada can be obtained from the ICH website (www.ich.org):

M4	Organization of the Common Technical Document for the Registration of Pharmaceuticals for Human Use
M4E (R1)	The Common Technical Document for the Registration of Pharmaceuticals for Human Use: Efficacy <ul style="list-style-type: none">• Clinical Overview and Clinical Summary of Module 2• Module 5: Clinical Study Reports
M4E (R4)	Implementation Working Group Questions and Answers
M4Q (R1)	The Common Technical Document for the Registration of Pharmaceuticals for Human Use: Quality <ul style="list-style-type: none">• Quality Overall Summary of Module 2• Module 3: Quality
M4Q (R1)	Implementation Working Group Questions and Answers
M4S (R2)	The Common Technical Document for the Registration of Pharmaceuticals for Human Use: Safety <ul style="list-style-type: none">• Non-Clinical Overview and Non-Clinical Summaries of Module 2• Organization of Module 4
M4S (R4)	Implementation Working Group Question and Answers

6.2 Other References

Uniform Requirements for Manuscripts Submitted to Biomedical Journals, International Committee of Medical Journals Editors (ICMJE) (<http://www.icmje.org/>)

Summary Technical Document (STED), developed by the Global Harmonization Task Force (GHTF)

(OECD) *Principles of Good Laboratory Practice (GLP)*